FIG.1

CCGGGTCGACCCACGCGTCCGAAGGCCCCCTCTCACTCCGCTCCACTCCTCGGGCTGG

5 CTCTCCTGAGGATGCACCAGCGTCACCCCCGGGCAAGATGCCCTCCCCTCTGTGTGGC

CGGAATCCTTGCCTGTGGCTTTCTCCTGGGCTGCTGGGGACCCTCCCATTTCCAGCAGA

GTTGTCTTCAGGCTTTGGAGCCACAGGCCGTGTCTTCTTACTTGAGCCCTGGTGCTCCC

TTAAAAGGCCGCCCTCCTTCCCCTGGCTTCCAGAGGCAGAGGCAGAGGCAGAGGCGGG

CTGCAGGCGGCATCCTACACCTGGAGCTGCTGGTGGCCGTGGGCCCCGATGTCTTCCA

10 GGCTCACCAGGAGGACACAGAGCGCTATGTGCTCACCAACCTCAACATCGGGGCAGAA

CTGCTTCGGGACCCGTCCCTGGGGGCTCAGTTTCGGGTGCACCTGGTGAAGATGGTCA

TTCTGACAGAGCCTGAGGGTGCTCCAAATATCACAGCCAACCTCACCTCGTCCCTGCTG

AGCGTCTGTGGGTGGAGCCAGACCATCAACCCTGAGGACGACACGGATCCTGGCCATG

CTGACCTGGTCCTCTATATCACTAGGTTTGACCTGGAGTTGCCTGATGGTAACCGGCAG

15 GTGCGGGGCGTCACCCAGCTGGGCGGTGCCTGCTCCCCAACCTGGAGCTGCCTCATTA

CCGAGGACACTGGCTTCGACCTGGGAGTCACCATTGCCCATGAGATTGGGCACAGCTT

CGGCCTGGAGCACGACGGCGCGCCCGGCAGCGGCTGCGGCCCCAGCGGACACGTGA

TGGCTTCGGACGGCGCCGCGCCCCGCGCCGGCCTCGCCTGGTCCCCCTGCAGCCGCC

GGCAGCTGCTGAGCCTGCTCAGCGCAGGACGGGCGCGCTGCGTGTGGGACCCGCCGC

20 GGCCTCAACCCGGGTCCGCGGGGCACCCGCCGGATGCGCAGCCTGGCCTCTACTACA

GCGCCAACGAGCAGTGCCGCGTGGCCTTCGGCCCCAAGGCTGTCGCCTGCACCTTCGC

CAGGGAGCACCTGGATATGTGCCAGGCCCTCTCCTGCCACACAGACCCGCTGGACCAA

AGCAGCTGCAGCCGCCTCCTCGTTCCTCTCCTGGATGGGACAGAATGTGGCGTGGAGA

AGTGGTGCTCCAAGGGTCGCTGCCGCTCCCTGGTGGAGCTGACCCCCATAGCAGCAGT

25 GCATGGGCGCTGGTCTAGCTGGGGTCCCCGAAGTCCTTGCTCCCGCTCCTGCGGAGGA

GGTGTGGTCACCAGGAGGCGGCAGTGCAACAACCCCAGACCTGCCTTTGGGGGGCGT

GCATGTGTTGGTGCTGACCTCCAGGCCGAGATGTGCAACACTCAGGCCTGCGAGAAGA

CCCAGCTGGAGTTCATGTCGCAACAGTGCGCCAGGACCGACGGCCAGCCGCTGCGCTC

CTCCCCTGGCGGCGCCTCCTTCTACCACTGGGGTGCTGCTGTACCACACAGCCAAGGG

30 GATGCTCTGTGCAGACACATGTGCCGGGCCATTGGCGAGAGCTTCATCATGAAGCGTG

GAGACAGCTTCCTCGATGGGACCGGTGTATGCCAAGTGGCCCCGGGAGGACGGGA

CCCTGAGCCTGTGTGTGTCGGGCAGCTGCAGGACATTTGGCTGTGATGGTAGGATGGA

CTCCCAGCAGGTATGGGACAGGTGCCAGGTGTGTGGTGGGGACAACAGCACGTGCAGC

CCACGGAAGGGCTCTTTCACAGCTGGCAGAGCGAGAGAATATGTCACGTTTCTGACAGT

35 TACCCCCAACCTGACCAGTGTCTACATTGCCAACCACAGGCCTCTCTTCACACACTTGG

CGGTGAGGATCGGAGGGCGCTATGTCGTGGCTGGGAAGATGAGCATCTCCCCTAACAC

CACCTACCCCTCCCTCCTGGAGGATGGTCGTGTCGAGTACAGAGTGGCCCTCACCGAG

GACCGGCTGCCCCGCCTGGAGGAGATCCGCATCTGGGGACCCCTCCAGGAAGATGCT
GACATCCAGGTTTACAGGCGGTATGGCGAGGAGTATGGCAACCTCACCCGCCCAGACA
TCACCTTCACCTACTTCCAGCCTAAGCCACGGCAGGCCTGGGTGTGGGCCGCTGTGCG
TGGGCCCTGCTCGGTGAGCTGTGGGGCAGGGCTGCGCTGGGTAAACTACAGCTGCCTG

5   GACCAGGCCAGGAAGGAGTTGGTGGAGACTGTCCAGTGCCAAGGGAGCCAGCAGCCA
CCAGCGTGGCCAGAGGCCTGCGTGCTCGAACCCTGCCCTCCCTACTGGGCGGTGGGA
GACTTCGGCCCATGCAGCGCCTCCTGTGGGGGTGGCCTGCGGGAGCGGCCAGTGCGC
TGCGTGGAGGCCCAGGGCAGCCTCCTGAAGACATTGCCCCCAGCCCGGTGCAGAGCA
GGGGCCCAGCAGCCAGCTGTGGCGCTGGAAACCTGCAACCCCCAGCCCTGCCCTGCC

10   AGGTGGGAGGTGTCAGAGCCCAGCTCATGCACATCAGCTGGTGGAGCAGGCCTGGCCT
TGGAGAACGAGACCTGTGTGCCAGGGGCAGATGGCCTGGAGGCTCCAGTGACTGAGG
GGCCTGGCTCCGTAGATGAGAAGCTGCCTGCCCCTGAGCCCTGTGTCGGGATGTCATG
TCCTCCAGGCTGGGGCCATCTGGATGCCACCTCTGCAGGGGAGAAGGCTCCCTCCCCA
TGGGGCAGCATCAGGACGGGGGCTCAAGCTGCACACGTGTGGACCCCTGCGGCAGGG

15   TCGTGCTCCGTCTCCTGCGGGCGAGGTCTGATGGAGCTGCGTTTCCTGTGCATGGACT
CTGCCCTCAGGGTGCCTGTCCAGGAAGAGCTGTGTGGCCTGGCAAGCAAGCCTGGGAG
CCGGCGGGAGGTCTGCCAGGCTGTCCCGTGCCCTGCTCGGTGGCAGTACAAGCTGGC
GGCCTGCAGCGTGAGCTGTGGGAGAGGGGTCGTGCGGAGGATCCTGTATTGTGCCCG
GGCCCATGGGGAGGACGATGGTGAGGAGATCCTGTTGGACACCCAGTGCCAGGGGCT

20   GCCTCGCCCGGAACCCCAGGAGGCCTGCAGCCTGGAGCCCTGCCCACCTAGGTGGAA
AGTCATGTCCCTTGGCCCATGTTCGGCCAGCTGTGGCCTTGGCACTGCTAGACGCTCG
GTGGCCTGTGTGCAGCTCGACCAAGGCCAGGACGTGGAGGTGGACGAGGCGGCCTGT
GCGGCGCTGGTGCGGCCCGAGGCCAGTGTCCCCTGTCTCATTGCCGACTGCACCTACC
GCTGGCATGTTGGCACCTGGATGGAGTGCTCTGTTTCCTGTGGGGATGGCATCCAGCG

25   CCGGCGTGACACCTGCCTCGGACCCCAGGCCCAGGCGCCTGTGCCAGCTGATTTCTGC
CAGCACTTGCCCAAGCCGGTGACTGTGCGTGGCTGCTGGGCTGGGCCCTGTGTGGGAC
AGGGTACGCCCAGCCTGGTGCCCCACGAAGAAGCCGCTGCTCCAGGACGGACCACAG
CCACCCCTGCTGGTGCCTGTGGCAGGCAGCACCTTGAGCCAACAGGAACCATTGACAT
GCGAGGCCCAGGGCAGGCAGACTGTGCAGTGGCCATTGGGCGGCCCCTCGGGGAGGT

30   GGTGACCCTCCGCGTCCTTGAGAGTTCTCTCAACTGCAGTGCGGGGGACATGTTGCTG
CTTTGGGGCCGGCTCACCTGGAGGAAGATGTGCAGGAAGCTGTTGGACATGACTTTCA
GCTCCAAGACCAACACGCTGGTGGTGAGGCAGCGCTGCGGGCGGCCAGGAGGTGGGG
TGCTGCTGCGGTATGGGAGCCAGCTTGCTCCTGAAACCTTCTACAGAGAATGTGACATG
CAGCTCTTTGGGCCCTGGGGTGAAATCGTGAGCCCCTCGCTGAGTCCAGCCACGAGTA

35   ATGCAGGGGGCTGCCGGCTCTTCATTAATGTGGCTCCGCACGCACGGATTGCCATCCAT
GCCCTGGCCACCAACATGGGCGCTGGGACCGAGGGAGCCAATGCCAGCTACATCTTGA
TCCGGGACACCCACAGCTTGAGGACCACAGCGTTCCATGGGCAGCAGGTGCTCTACTG

GGAGTCAGAGAGCAGCCAGGCTGAGATGGAGTTCAGCGAGGGCTTCCTGAAGGCTCAG
GCCAGCCTGCGGGGCCAGTACTGGACCCTCCAATCATGGGTACCGGAGATGCAGGACC
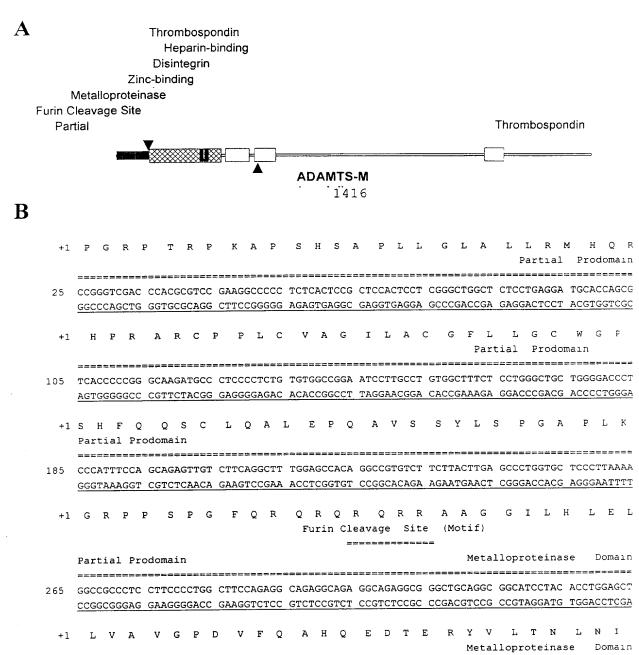CTCAGTCCTGGAAGGGAAAGGAAGGAACC

FIG. 2

5

PGRPTRPKAPSHSAPLLGLALLRMHQRHPRARCPPLCVAGILACGFLLGCWGPSHFQQSCL
QALEPQAVSSYLSPGAPLKGRPPSPGFQRQRQRQRRAAGGILHLELLVAVGPDVFQAHQED
TERYVLTNLNIGAELLRDPSLGAQFRVHLVKMVILTEPEGAPNITANLTSSLLSVCGWSQTINP
EDDTDPGHADLVLYITRFDLELPDGNRQVRGVTQLGGACSPTWSCLITEDTGFDLGVTIAHEI

10   GHSFGLEHDGAPGSGCGPSGHVMASDGAAPRAGLAWSPCSRRQLLSLLSAGRARCVWDP
PRPQPGSAGHPPDAQPGLYYSANEQCRVAFGPKAVACTFAREHLDMCQALSCHTDPLDQS
SCSRLLVPLLDGTECGVEKWCSKGRCRSLVELTPIAAVHGRWSSWGPRSPCSRSCGGGVV
TRRRQCNNPRPAFGGRACVGADLQAEMCNTQACEKTQLEFMSQQCARTDGQPLRSSPGG
ASFYHWGAAVPHSQGDALCRHMCRAIGESFIMKRGDSFLDGTRCMPSGPREDGTLSLCVS

15   GSCRTFGCDGRMDSQQVWDRCQVCGGDNSTCSPRKGSFTAGRAREYVTFLTVTPNLTSV
YIANHRPLFTHLAVRIGGRYVVAGKMSISPNTTYPSLLEDGRVEYRVALTEDRLPRLEEIRIWG
PLQEDADIQVYRRYGEEYGNLTRPDITFTYFQPKPRQAWVWAAVRGPCSVSCGAGLRWVN
YSCLDQARKELVETVQCQGSQQPPAWPEACVLEPCPPYWAVGDFGPCSASCGGGLRERP
VRCVEAQGSLLKTLPPARCRAGAQQPAVALETCNPQPCPARWEVSEPSSCTSAGGAGLAL

20   ENETCVPGADGLEAPVTEGPGSVDEKLPAPEPCVGMSCPPGWGHLDATSAGEKAPSPWG
SIRTGAQAAHVWTPAAGSCSVSCGRGLMELRFLCMDSALRVPVQEELCGLASKPGSRREV
CQAVPCPARWQYKLAACSVSCGRGVVRRILYCARAHGEDDGEEILLDTQCQGLPRPEPQE
ACSLEPCPPRWKVMSLGPCSASCGLGTARRSVACVQLDQGQDVEVDEAACAALVRPEASV
PCLIADCTYRWHVGTWMECSVSCGDGIQRRRDTCLGPQAQAPVPADFCQHLPKPVTVRGC

25   WAGPCVGQGTPSLVPHEEAAAPGRTTATPAGACGRQHLEPTGTIDMRGPGQADCAVAIGR
PLGEVVTLRVLESSLNCSAGDMLLLWGRLTWRKMCRKLLDMTFSSKTNTLVVRQRCGRPG
GGVLLRYGSQLAPETFYRECDMQLFGPWGEIVSPSLSPATSNAGGCRLFINVAPHARIAIHAL
ATNMGAGTEGANASYILIRDTHSLRTTAFHGQQVLYWESESSQAEMEFSEGFLKAQASLRG
QYWTLQSWVPEMQDPQSWKGKEGT

30

Figure 3

Domain structure of ADAMTS-M and translated nucleic acid sequence. A) Diagram of ADAMTS-M showing the following domains and signature motifs (with amino acid numbers in parentheses): partial prodomain (1-97), furin cleavage site (94-97), metalloproteinase domain (98-311), zinc-binding motif (247-272), disintegrin domain (324-394), thrombospondin submotifs (410-473 and 1099-1156), and a heparin-binding motif (419-424). B) ADAMTS-M nucleotide sequence with translated amino acid sequence above.

A

ADAMTS-M
1416

B

```
+1   P  G  R  P   T  R  P   K  A  P   S  H  S  A   P  L  L   G  L  A   L  L  R  M   H  Q  R
                                                              Partial  Prodomain

     ================================================================================

25   CCGGGTCGAC CCACGCGTCC GAAGGCCCCC TCTCACTCCG CTCCACTCCT CGGGCTGGCT CTCCTGAGGA TGCACCAGCG
     GGCCCAGCTG GGTGCGCAGG CTTCCGGGGG AGAGTGAGGC GAGGTGAGGA GCCCGACCGA GAGGACTCCT ACGTGGTCGC


+1   H  P  R   A  R  C  P   P  L  C   V  A  G   I  L  A  C   G  F   L  G  C   W  G  F
                                                              Partial  Prodomain

     ================================================================================

105  TCACCCCCGG GCAAGATGCC CTCCCCTCTG TGTGGCCGGA ATCCTTGCCT GTGGCTTTCT CCTGGGCTGC TGGGGACCCT
     AGTGGGGGCC CGTTCTACGG GAGGGGAGAC ACACCGGCCT TAGGAACGGA CACCGAAAGA GGACCCGACG ACCCCTGGGA


+1   S  H  F  Q   Q  S  C   L  Q  A  L   E  P  Q   A  V  S   S  Y  L  S   P  G  A   P  L  K
     Partial Prodomain

     ================================================================================

185  CCCATTTCCA GCAGAGTTGT CTTCAGGCTT TGGAGCCACA GGCCGTGTCT TCTTACTTGA GCCCTGGTGC TCCCTTAAAA
     GGGTAAAGGT CGTCTCAACA GAAGTCCGAA ACCTCGGTGT CCGGCACAGA AGAATGAACT CGGGACCACG AGGGAATTTT


+1   G  R  P  P   S  P  G   F  Q  R   Q  R  Q  R   Q  R  R   A  A  G   G  I  L  H   L  E  L
                             Furin Cleavage  Site  (Motif)

                             ================

     Partial Prodomain                                      Metalloproteinase   Domain

     ================================================================================

265  GGCCGCCCTC CTTCCCCTGG CTTCCAGAGG CAGAGGCAGA GGCAGAGGCG GGCTGCAGGC GGCATCCTAC ACCTGGAGCT
     CCGGCGGGAG GAAGGGGACC GAAGGTCTCC GTCTCCGTCT CCGTCTCCGC CCGACGTCCG CCGTAGGATG TGGACCTCGA


+1   L  V  A   V  G  P  D   V  F  Q   A  H  Q   E  D  T  E   R  Y  V   L  T  N   L  N  I
                                                              Metalloproteinase   Domain

     ================================================================================

345  GCTGGTGGCC GTGGGCCCCG ATGTCTTCCA GGCTCACCAG GAGGACACAG AGCGCTATGT GCTCACCAAC CTCAACATCG
     CGACCACCGG CACCCGGGGC TACAGAAGGT CCGAGTGGTC CTCCTGTGTC TCGCGATACA CGAGTGGTTG GAGTTGTAGC
```

```
 +1 G  A  E  L   L  R  D   P  S  L  G   A  Q  F   R  V  H   L  V  K  M   V  I  L    T  E  P
                                                          Metalloproteinase   Domain
    ================================================================================
425 GGGCAGAACT GCTTCGGGAC CCGTCCCTGG GGGCTCAGTT TCGGGTGCAC CTGGTGAAGA TGGTCATTCT GACAGAGCCT
    CCCGTCTTGA CGAAGCCCTG GGCAGGGACC CCCGAGTCAA AGCCCACGTG GACCACTTCT ACCAGTAAGA CTGTCTCGGA


 +1 E  G  A  P   N  I  T   A  N  L   T  S  S  L   L  S  V   C  G  W   S  Q  T   I   N  P  E
                                                          Metalloproteinase   Domain
    ================================================================================
505 GAGGGTGCTC CAAATATCAC AGCCAACCTC ACCTCGTCCC TGCTGAGCGT CTGTGGGTGG AGCCAGACCA TCAACCCTGA
    CTCCCACGAG GTTTATAGTG TCGGTTGGAG TGGAGCAGGG ACGACTCGCA GACACCCACC TCGGTCTGGT AGTTGGGACT


 +1  D  D  T   D  P  G  H   A  D  L   V  L  Y   I  T  R  F   D  L  E   L  P   D   G  N  R
                                       Metalloproteinase   Domain
    ================================================================================
585 GGACGACACG GATCCTGGCC ATGCTGACCT GGTCCTCTAT ATCACTAGGT TTGACCTGGA GTTGCCTGAT GGTAACCGGC
    CCTGCTGTGC CTAGGACCGG TACGACTGGA CCAGGAGATA TAGTGATCCA AACTGGACCT CAACGGACTA CCATTGGCCG


 +1 Q  V  R  G   V  T  Q   L  G  G  A   C  S  P   T  W  S   C  L  I  T   E  D  T   G  F  D
    Metalloproteinase   Domain
    ================================================================================
665 AGGTGCGGGG CGTCACCCAG CTGGGCGGTG CCTGCTCCCC AACCTGGAGC TGCCTCATTA CCGAGGACAC TGGCTTCGAC
    TCCACGCCCC GCAGTGGGTC GACCCGCCAC GGACGAGGGG TTGGACCTCG ACGGAGTAAT GGCTCCTGTG ACCGAAGCTG


 +1 L  G  V  T   I  A  H   E  I  G   H  S  F  G   L  E  H   D  G  A   P  G  S   C  G  P
                                                          Zinc-binding   Motif
                               ================================================
    Metalloproteinase   Domain
    ================================================================================
745 CTGGGAGTCA CCATTGCCCA TGAGATTGGG CACAGCTTCG GCCTGGAGCA CGACGGCGCG CCCGGCAGCG GCTGCGGCCC
    GACCCTCAGT GGTAACGGGT ACTCTAACCC GTGTCGAAGC CGGACCTCGT GCTGCCGCGC GGGCCGTCGC CGACGCCGGG


 +1  S  G  H   V  M  A  S   D  G  A   A  P  R   A  G  L  A   W  S  P   C  S  R   R  Q  L
    Zinc-binding   Motif
    ==================
    Metalloproteinase   Domain
    ================================================================================
825 CAGCGGACAC GTGATGGCTT CGGACGGCGC CGCGCCCCGC GCCGGCCTCG CCTGGTCCCC CTGCAGCCGC CGGCAGCTGC
    GTCGCCTGTG CACTACCGAA GCCTGCCGCG GCGCGGGGCG CGGCCGGAGC GGACCAGGGG GACGTCGGCG GCCGTCGACG


 +1 L  S  L  L   S  A  G   R  A  R  C   V  W  D   P  P  R   P  Q  P  G   S  A  G   H  P  P
    Metalloproteinase   Domain
    ==========================================================
905 TGAGCCTGCT CAGCGCAGGA CGGGCGCGCT GCGTGTGGGA CCCGCCGCGG CCTCAACCCG GGTCCGCGGG GCACCCGCCG
    ACTCGGACGA GTCGCGTCCT GCCCGCGCGA CGCACACCCT GGGCGGCGCC GGAGTTGGGC CCAGGCGCCC CGTGGGCGGC


 +1 D  A  Q  P   G  L  Y   Y  S  A   N  E  Q  C   R  V  A   F  G  P   K  A  V  A   C  T  F
                                                                     Disintegrin   Domain
    ================================================================================
985 GATGCGCAGC CTGGCCTCTA CTACAGCGCC AACGAGCAGT GCCGCGTGGC CTTCGGCCCC AAGGCTGTCG CCTGCACCTT
    CTACGCGTCG GACCGGAGAT GATGTCGCGG TTGCTCGTCA CGGCGCACCG GAAGCCGGGG TTCCGACAGC GGACGTGGAA
```

```
+1    A   R   E   H   L   D   M   C   Q   A   L   S   C   H   T   D   P   L   D   Q   S   S   C   S   R   L
                              Disintegrin  Domain
      ==================================================================================================
1065  CGCCAGGGAG CACCTGGATA TGTGCCAGGC CCTCTCCTGC CACACAGACC CGCTGGACCA AAGCAGCTGC AGCCGCCTCC
      GCGGTCCCTC GTGGACCTAT ACACGGTCCG GGAGAGGACG GTGTGTCTGG CGACCTGGT TTCGTCGACG TCGGCGGAGG


+1 L   V   P   L   L   D   G   T   E   C   G   V   E   K   W   C   S   K   G   R   C   R   S   L   V   E   L
   Disintegrin  Domain
   =================================================================================================
1145  TCGTTCCTCT CCTGGATGGG ACAGAATGTG GCGTGGAGAA GTGGTGCTCC AAGGGTCGCT GCCGCTCCCT GGTGGAGCTG
      AGCAAGGAGA GGACCTACCC TGTCTTACAC CGCACCTCTT CACCACGAGG TTCCCAGCGA CGGCGAGGGA CCACCTCGAC


+1    T   P   I   A   A   V   H   G   R   W   S   S   W   G   P   R   S   P   C   S   R   S   C   G   G   V
                                                             Heparin-binding  Motif
                                                             =====================
                                                             Thrombospondin    Submotif
      ==================================================================================================
1225  ACCCCCATAG CAGCAGTGCA TGGGCGCTGG TCTAGCTGGG GTCCCCGAAG TCCTTGCTCC CGCTCCTGCG GAGGAGGTGT
      TGGGGGTATC GTCGTCACGT ACCCGCGACC AGATCGACCC CAGGGGCTTC AGGAACGAGG GCGAGGACGC CTCCTCCACA


+1    V   T   R   R   R   Q   C   N   N   P   R   P   A   F   G   G   R   A   C   V   G   A   D   L   Q   A
                              Thrombospondin  Submotif
      ==================================================================================================
1305  GGTCACCAGG AGGCGGCAGT GCAACAACCC CAGACCTGCC TTTGGGGGGC GTGCATGTGT TGGTGCTGAC CTCCAGGCCG
      CCAGTGGTCC TCCGCCGTCA CGTTGTTGGG GTCTGGACGG AAACCCCCCG CACGTACACA ACCACGACTG GAGGTCCGGC


+1 E   M   C   N   T   Q   A   C   E   K   T   Q   L   E   F   M   S   Q   Q   C   A   R   T   D   G   Q   P
   Thrombospondin  Submotif
   =================================================================================
1385  AGATGTGCAA CACTCAGGCC TGCGAGAAGA CCCAGCTGGA GTTCATGTCG CAACAGTGCG CCAGGACCGA CGGCCAGCCG
      TCTACACGTT GTGAGTCCGG ACGCTCTTCT GGGTCGACCT CAAGTACAGC GTTGTCACGC GGTCCTGGCT GCCGGTCGGC


+1    L   R   S   S   P   G   G   A   S   F   Y   H   W   G   A   A   V   P   H   S   Q   G   D   A   L   C   R
1465  CTGCGCTCCT CCCCTGGCGG CGCCTCCTTC TACCACTGGG GTGCTGCTGT ACCACACAGC CAAGGGGATG CTCTGTGCAG
      GACGCGAGGA GGGGACCGCC GCGGAGGAAG ATGGTGACCC CACGACGACA TGGTGTGTCG GTTCCCCTAC GAGACACGTC


+1    H   M   C   R   A   I   G   E   S   F   I   M   K   R   G   D   S   F   L   D   G   T   R   C   M   P
1545  ACACATGTGC CGGGCCATTG GCGAGAGCTT CATCATGAAG CGTGGAGACA GCTTCCTCGA TGGGACCCGG TGTATGCCAA
      TGTGTACACG GCCCGGTAAC CGCTCTCGAA GTAGTACTTC GCACCTCTGT CGAAGGAGCT ACCCTGGGCC ACATACGGTT


+1 S   G   P   R   E   D   G   T   L   S   L   C   V   S   G   S   C   R   T   F   G   C   D   G   R   M   D
1625  GTGGCCCCCG GGAGGACGGG ACCCTGAGCC TGTGTGTGTC GGGCAGCTGC AGGACATTTG GCTGTGATGG TAGGATGGAC
      CACCGGGGGC CCTCCTGCCC TGGGACTCGG ACACACACAG CCCGTCGACG TCCTGTAAAC CGACACTACC ATCCTACCTG


+1 S   Q   Q   V   W   D   R   C   Q   V   C   G   G   D   N   S   C   S   P   R   K   G   S   F   T   A
1705  TCCCAGCAGG TATGGGACAG GTGCCAGGTG TGTGGTGGGG ACAACAGCAC GTGCAGCCCA CGGAAGGGCT CTTTCACAGC
      AGGGTCGTCC ATACCCTGTC CACGGTCCAC ACACCACCCC TGTTGTCGTG CACGTCGGGT GCCTTCCCGA GAAAGTGTCG


+1    G   R   A   R   E   Y   V   T   F   L   T   V   T   P   N   L   T   S   V   Y   I   A   N   H   R   P
1785  TGGCAGAGCG AGAGAATATG TCACGTTTCT GACAGTTACC CCCAACCTGA CCAGTGTCTA CATTGCCAAC CACAGGCCTC
      ACCGTCTCGC TCTCTTATAC AGTGCAAAGA CTGTCAATGG GGGTTGGACT GGTCACAGAT GTAACGGTTG GTGTCCGGAG
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```
  +1 L  F  T  H   L  A  V  R   I  G  G   R  Y  V   V  A  G   K  M  S   I  S   P  N   T  T  Y
1865 TCTTCACACA CTTGGCGGTG AGGATCGGAG GGCGCTATGT CGTGGCTGGG AAGATGAGCA TCTCCCCTAA CACCACCTAC
     AGAAGTGTGT GAACCGCCAC TCCTAGCCTC CCGCGATACA GCACCGACCC TTCTACTCGT AGAGGGGATT GTGGTGGATG


  +1 P  S  L  L   E  D  G   R  V  E   Y  R  V   A  L  T  E   D  R  L   P  R  L  E   E  I  R
1945 CCCTCCCTCC TGGAGGATGG TCGTGTCGAG TACAGAGTGG CCCTCACCGA GGACCGGCTG CCCCGCCTGG AGGAGATCCG
     GGGAGGGAGG ACCTCCTACC AGCACAGCTC ATGTCTCACC GGGAGTGGCT CCTGGCCGAC GGGGCGGACC TCCTCTAGGC


  +1  I  W  G   P  L  Q  E   D  A  D   I  Q  V   Y  R  R  Y   G  E  E   Y  G  N   L  T  R
2025 CATCTGGGGA CCCCTCCAGG AAGATGCTGA CATCCAGGTT TACAGGCGGT ATGGCGAGGA GTATGGCAAC CTCACCCGCC
     GTAGACCCCT GGGGAGGTCC TTCTACGACT GTAGGTCCAA ATGTCCGCCA TACCGCTCCT CATACCGTTG GAGTGGGCGG


  +1 P  D  I  T   F  T  Y   F  Q  P  K   P  R  Q   A  W  V   W  A  A  V   R  G  P   C  S  V
2105 CAGACATCAC CTTCACCTAC TTCCAGCCTA AGCCACGGCA GGCCTGGGTG TGGGCCGCTG TGCGTGGGCC CTGCTCGGTG
     GTCTGTAGTG GAAGTGGATG AAGGTCGGAT TCGGTGCCGT CCGGACCCAC ACCCGGCGAC ACGCACCCGG GACGAGCCAC


  +1 S  C  G  A   G  L  R   W  V  N   Y  S  C  L   D  Q  A   R  K  E   L  V  E  T   V  Q  C
2185 AGCTGTGGGG CAGGGCTGCG CTGGGTAAAC TACAGCTGCC TGGACCAGGC CAGGAAGGAG TTGGTGGAGA CTGTCCAGTG
     TCGACACCCC GTCCCGACGC GACCCATTTG ATGTCGACGG ACCTGGTCCG GTCCTTCCTC AACCACCTCT GACAGGTCAC


  +1 Q  G  S   Q  Q  P  P   A  W  P   E  A  C   V  L  E  P   C  P  P   Y  W  A   V  G  D
2265 CCAAGGGAGC CAGCAGCCAC CAGCGTGGCC AGAGGCCTGC GTGCTCGAAC CCTGCCCTCC CTACTGGGCG GTGGGAGACT
     GGTTCCCTCG GTCGTCGGTG GTCGCACCGG TCTCCGGACG CACGAGCTTG GGACGGGAGG GATGACCCGC CACCCTCTGA


  +1 F  G  P  C   S  A  S   C  G  G  G   L  R  E   R  P  V   R  C  V   E  A  Q  G   S  L  L
2345 TCGGCCCATG CAGCGCCTCC TGTGGGGGTG GCCTGCGGGA GCGGCCAGTG CGCTGCGTGG AGGCCCAGGG CAGCCTCCTG
     AGCCGGGTAC GTCGCGGAGG ACACCCCCAC CGGACGCCCT CGCCGGTCAC GCGACGCACC TCCGGGTCCC GTCGGAGGAC


  +1 K  T  L  P   P  A  R   C  R  A   G  A  Q  Q   P  A  V   A  L  E   T  C  N  P   Q  P  C
2425 AAGACATTGC CCCCAGCCCG GTGCAGAGCA GGGGCCCAGC AGCCAGCTGT GGCGCTGGAA ACCTGCAACC CCCAGCCCTG
     TTCTGTAACG GGGGTCGGGC CACGTCTCGT CCCCGGGTCG TCGGTCGACA CCGCGACCTT TGGACGTTGG GGGTCGGGAC


  +1  P  A  R   W  E  V  S   E  P  S   S  C  T   S  A  G  G   A  G  L   A  L  E   N  E  T
2505 CCCTGCCAGG TGGGAGGTGT CAGAGCCCAG CTCATGCACA TCAGCTGGTG GAGCAGGCCT GGCCTTGGAG AACGAGACCT
     GGGACGGTCC ACCCTCCACA GTCTCGGGTC GAGTACGTGT AGTCGACCAC CTCGTCCGGA CCGGAACCTC TTGCTCTGGA


  +1 C  V  P  G   A  D  G   L  E  A  P   V  T  E   G  P  G   S  V  D   E  K  L  P   A  P  E
2585 GTGTGCCAGG GGCAGATGGC CTGGAGGCTC CAGTGACTGA GGGGCCTGGC TCCGTAGATG AGAAGCTGCC TGCCCCTGAG
     CACACGGTCC CCGTCTACCG GACCTCCGAG GTCACTGACT CCCCGGACCG AGGCATCTAC TCTTCGACGG ACGGGGACTC


  +1 P  C  V  G   M  S  C   P  P  G   W  G  H  L   D  A  T   S  A  G   E  K  A  P   S  P  W
2665 CCCTGTGTCG GGATGTCATG TCCTCCAGGC TGGGGCCATC TGGATGCCAC CTCTGCAGGG GAGAAGGCTC CCTCCCCATG
     GGGACACAGC CCTACAGTAC AGGAGGTCCG ACCCCGGTAG ACCTACGGTG GAGACGTCCC CTCTTCCGAG GGAGGGGTAC


  +1 G. S  I   R  T  G  A   Q  A  A   H  V  W   T  P  A  A   G  S  C   S  V  S   C  G  R
2745 GGGCAGCATC AGGACGGGGG CTCAAGCTGC ACACGTGTGG ACCCCTGCGG CAGGGTCGTG CTCCGTCTCC TGCGGGCGAG
     CCCGTCGTAG TCCTGCCCCC GAGTTCGACG TGTGCACACC TGGGGACGCC GTCCCAGCAC GAGGCAGAGG ACGCCCGCTC


  +1 G  L  M  E   L  R  F   L  C  M  D   S  A  L   R  V  P   V  Q  E   E  L  C  G   L  A  S
2825 GTCTGATGGA GCTGCGTTTC CTGTGCATGG ACTCTGCCCT CAGGGTGCCT GTCCAGGAAG AGCTGTGTGG CCTGGCAAGC
     CAGACTACCT CGACGCAAAG GACACGTACC TGAGACGGGA GTCCCACGGA CAGGTCCTTC TCGACACACC GGACCGTTCG
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     +1    K  P  G  S  R  R  E    V  C  Q    A  V  P  C    P  A  R    W  Q  Y    K  L  A  A    C  S  \
     2905  AAGCCTGGGA GCCGGCGGGA GGTCTGCCAG GCTGTCCCGT GCCCTGCTCG GTGGCAGTAC AAGCTGGCGG CCTGCAGCGT
           TTCGGACCCT CGGCCGCCCT CCAGACGGTC CGACAGGGCA CGGGACGAGC CACCGTCATG TTCGACCGCC GGACGTCGCA


     +1    S  C  G    R  G  V  V    R  R  I    L  Y  C    A  R  A  H    G  E  D    D  G  E    E  I  L
     2985  GAGCTGTGGG AGAGGGGTCG TGCGGAGGAT CCTGTATTGT GCCCGGGCCC ATGGGGAGGA CGATGGTGAG GAGATCCTGT
           CTCGACACCC TCTCCCCAGC ACGCCTCCTA GGACATAACA CGGGCCCGGG TACCCCTCCT GCTACCACTC CTCTAGGACA


     +1    L  D  T  Q    C  Q  G    L  P  R  P    E  P  Q    E  A  C    S  L  E  P    C  P  P    R  W  K
     3065  TGGACACCCA GTGCCAGGGG CTGCCTCGCC CGGAACCCCA GGAGGCCTGC AGCCTGGAGC CTGCCCACC TAGGTGGAAA
           ACCTGTGGGT CACGGTCCCC GACGGAGCGG GCCTTGGGGT CCTCCGGACG TCGGACCTCG GACGGGTGG ATCCACCTTT


     +1    V  M  S  L    G  P  C    S  A  S    C  G  L  G    T  A  R    R  S  V    A  C  V  Q    L  D  Q
     3145  GTCATGTCCC TTGGCCCATG TTCGGCCAGC TGTGGCCTTG GCACTGCTAG ACGCTCGGTG GCCTGTGTGC AGCTCGACCA
           CAGTACAGGG AACCGGGTAC AAGCCGGTCG ACACCGGAAC CGTGACGATC TGCGAGCCAC CGGACACACG TCGAGCTGGT


     +1     G  Q  D    V  E  V  D    E  A  A    C  A  A    L  V  R  P    E  A  S    V  P  C    L  I  A
     3225  AGGCCAGGAC GTGGAGGTGG ACGAGGCGGC CTGTGCGGCG CTGGTGCGGC CCGAGGCCAG TGTCCCCTGT CTCATTGCCG
           TCCGGTCCTG CACCTCCACC TGCTCCGCCG GACACGCCGC GACCACGCCG GGCTCCGGTC ACAGGGGACA GAGTAACGGC


     +1    D  C  T  Y    R  W  H    V  G  T  W    M  E  C    S  V  S    C  G  D  G    I  Q  R    R  R  D
                                                                        Thrombospondin   Submotif
           =======================================================================================
     3305  ACTGCACCTA CCGCTGGCAT GTTGGCACCT GGATGGAGTG CTCTGTTTCC TGTGGGGATG GCATCCAGCG CCGGCGTGAC
           TGACGTGGAT GGCGACCGTA CAACCGTGGA CCTACCTCAC GAGACAAAGG ACACCCCTAC CGTAGGTCGC GGCCGCACTG


     +1    T  C  L  G    P  Q  A    Q  A  P    V  P  A  D    F  C  Q    H  L  P    K  P  V  T    V  R  G
                          Thrombospondin    Submotif
           =======================================================================================
     3385  ACCTGCCTCG GACCCCAGGC CCAGGCGCCT GTGCCAGCTG ATTTCTGCCA GCACTTGCCC AAGCCGGTGA CTGTGCGTGG
           TGGACGGAGC CTGGGGTCCG GGTCCGCGGA CACGGTCGAC TAAAGACGGT CGTGAACGGG TTCGGCCACT GACACGCACC


     +1    C  W  A    G  P  C  V    G  Q  G    T  P  S    L  V  P  H    E  E  A    A  A  P    G  R  T
           Thrombospondin   Submotif
           ================================
     3465  CTGCTGGGCT GGGCCCTGTG TGGGACAGGG TACGCCCAGC CTGGTGCCCC ACGAAGAAGC CGCTGCTCCA GGACGGACCA
           GACGACCCGA CCCGGGACAC ACCCTGTCCC ATGCGGGTCG GACCACGGGG TGCTTCTTCG GCGACGAGGT CCTGCCTGGT


     +1  T  A  T  P    A  G  A    C  G  R  Q    H  L  E    P  T  G    T  I  D  M    R  G  P    G  Q  A
     3545  CAGCCACCCC TGCTGGTGCC TGTGGCAGGC AGCACCTTGA GCCAACAGGA ACCATTGACA TGCGAGGCCC AGGGCAGGCA
           GTCGGTGGGG ACGACCACGG ACACCGTCCG TCGTGGAACT CGGTTGTCCT TGGTAACTGT ACGCTCCGGG TCCCGTCCGT


     +1   D  C  A  V    A  I  G    R  P  L    G  E  V  V    T  L  R    V  L  E    S  S  L  N    C  S  A
     3625  GACTGTGCAG TGGCCATTGG GCGGCCCCTC GGGGAGGTGG TGACCCTCCG CGTCCTTGAG AGTTCTCTCA ACTGCAGTGC
           CTGACACGTC ACCGGTAACC CGCCGGGGAG CCCCTCCACC ACTGGGAGGC GCAGGAACTC TCAAGAGAGT TGACGTCACG


     +1    G  D  M    L  L  L  W    G  R  L    T  W  R    K  M  C  R    K  L  L    D  M  T    F  S  S
     3705  GGGGGACATG TTGCTGCTTT GGGGCCGGCT CACCTGGAGG AAGATGTGCA GGAAGCTGTT GGACATGACT TTCAGCTCCA
           CCCCCTGTAC AACGACGAAA CCCCGGCCGA GTGGACCTCC TTCTACACGT CCTTCGACAA CCTGTACTGA AAGTCGAGGT


     +1  K  T  N  T    L  V  V    R  Q  R  C    G  R  P    G  G  G    V  L  L  R    Y  G  S    Q  L  A
     3785  AGACCAACAC GCTGGTGGTG AGGCAGCGCT GCGGGCGGCC AGGAGGTGGG GTGCTGCTGC GGTATGGGAG CCAGCTTGCT
           TCTGGTTGTG CGACCACCAC TCCGTCGCGA CGCCCGCCGG TCCTCCACCC CACGACGACG CCATACCCTC GGTCGAACGA
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  +1   P   E   T   F   Y   R   E    C   D   M    Q   L   F   G    P   W   G    E   I   V    S   P   S   L    S   P   A
3865   CCTGAAACCT TCTACAGAGA ATGTGACATG CAGCTCTTTG GGCCCTGGGG TGAAATCGTG AGCCCCTCGC TGAGTCCAGC
       GGACTTTGGA AGATGTCTCT TACACTGTAC GTCGAGAAAC CCGGGACCCC ACTTTAGCAC TCGGGGAGCG ACTCAGGTCG


  +1   T   S   N    A   G   G   C    R   L   F    I   N   V    A   P   H   A    R   I   A    I   H   A    L   A   T
3945   CACGAGTAAT GCAGGGGGCT GCCGGCTCTT CATTAATGTG GCTCCGCACG CACGGATTGC CATCCATGCC CTGGCCACCA
       GTGCTCATTA CGTCCCCCGA CGGCCGAGAA GTAATTACAC CGAGGCGTGC GTGCCTAACG GTAGGTACGG GACCGGTGGT


  +1 N M   G   A    G   T   E    G   A   N   A    S   Y   I    L   I   R    D   T   H   S    L   R   T    T   A   F
4025   ACATGGGCGC TGGGACCGAG GGAGCCAATG CCAGCTACAT CTTGATCCGG GACACCCACA GCTTGAGGAC CACAGCGTTC
       TGTACCCGCG ACCCTGGCTC CCTCGGTTAC GGTCGATGTA GAACTAGGCC CTGTGGGTGT CGAACTCCTG GTGTCGCAAG


  +1   H   G   Q   Q    V   L   Y    W   E   S    E   S   S   Q    A   E   M    E   F   S    E   G   F    L   K   A   Q
4105   CATGGGCAGC AGGTGCTCTA CTGGGAGTCA GAGAGCAGCC AGGCTGAGAT GGAGTTCAGC GAGGGCTTCC TGAAGGCTCA
       GTACCCGTCG TCCACGAGAT GACCCTCAGT CTCTCGTCGG TCCGACTCTA CCTCAAGTCG CTCCCGAAGG ACTTCCGAGT


  +1   A   S   L    R   G   Q   Y    W   T   L    Q   S   W    V   P   E   M    Q   D   P    Q   S   W    K   G   K
4185   GGCCAGCCTG CGGGGCCAGT ACTGGACCCT CCAATCATGG GTACCGGAGA TGCAGGACCC TCAGTCCTGG AAGGGAAAGG
       CCGGTCGGAC GCCCCGGTCA TGACCTGGGA GGTTAGTACC CATGGCCTCT ACGTCCTGGG AGTCAGGACC TTCCCTTTCC


  +1 E   G   T
4265   AAGGAACC
       TTCCTTGG
```

Fig. 4

Metalloproteinase Domain Alignment of ADAMTS-M v. ADAMTS Family

Percent Homology

	Sim	Ident
hADAMTS-4 (AB014588)	44	32
hADAMTS-5 (AF142099)	44	28
hADAMTS-1 (AF060152)	47	29
hADAMTS-8 (AF060153)	46	29
hADAMTS-2 (AJ003125)	49	32
	63	48

(TS-4 v. TS-5)

```
                    301                                                          360
hADAMTS-4 (AB014588)  (202) SPSPRRR--------BAKRFASLSRF-VETLLVVADDVMAAFHG-AGTKRYL VMAAAA
hADAMTS-5 (AF142099)  (241) QSALSPAGGSGPQTWMRRRSIRRARQ-VLLVARASMARLX-RGIQHLLLASEAN
hADAMTS-1 (AF060152)  (220) QGVGQRTGTGSI---RKRRVSHRY-VETLLVADQSMAEFHG-SGLKHYLTFSVAA
hADAMTS-8 (AF060153)  (199) ASEPPPPLGATS---RTKRFYSEARF-VETLLVADQSMAAFYG-ADLQNHLNSVAA
hADAMTS-2 (AJ003125)  (248) EHANSSR--R----RARRHAADDYNIFVLLGVDSVVQFIGKEHVQKHLMMLLVN
              M1-MPD   (1)  --------------AAMGILH-LMIVAVGPVFQARQ-EDTERVLNLNLGA
           Consensus  (301)               R  KRFAS  R  VETLLVAD SMA FHG   GLQ YLLTLMSIAA
                    361                                                          420
hADAMTS-4 (AB014588)  (251) KAFKHPFRNPVSIVYTRLVILGGEEQGWGP-SAQTRSFCA QRGLNTEEDSDPDH
hADAMTS-5 (AF142099)  (299) RLYSHALENHIRIAYVGVVGLGKDKSLVSK-NATTTRNSLKIHQHNQLGIDHEEH
hADAMTS-1 (AF060152)  (274) KLVKHPFRNSVSVSIVVKILVTHDEQKGPBVTS-NALTIRNKQOHNPPSPROAEH
hADAMTS-8 (AF060153)  (253) RLYKHPFKNSINLNVVKIIVKDEKWGPEVSD-NGGLVRNFNLRRFNQFSDHAPEH
hADAMTS-2 (AJ003125)  (300) ELVHDELGAHINVINVINRILILSYGKSMSLIEIGNPSQSLIEVVRRAYLQQKPDTGHDEY
              M1-MPD   (39) BLLRDELGAQFRVHLVRMVAITEPEGARVITA-ILTSHLEVLGSQTINPEDDTDRGH
           Consensus  (361) RLYKHPSI N I LVVVK VIL D   GPEV    NAA TLRNFC WQ    N P  D HPEH
                    421                                                          480
hADAMTS-4 (AB014588)  (310) FTAILRMADVGTVCDLL-VSTCDTHRADVGTVIARALYEDDLCSAFTA
hADAMTS-5 (AF142099)  (358) RRALIKMEDLCG-HHSCDTLGRADVGNISERAVEDDHHATTVIT LLG
hADAMTS-1 (AF060152)  (333) YFALLIQDDLCG-SQTCDTLGMADVGNVDSSLSVEDDELQOAFTTLHLVEN
hADAMTS-8 (AF060153)  (312) YFALLIRQNFGCQEGLCDTLGMLVDIGIINRSYEDELQOARHLLAHELGVLS
hADAMTS-2 (AJ003125)  (360) HAIELGQDHGP-SG---MQFYAPNTGMLVELTLNIEDFSSANVVIIVLG
              M1-MPD   (98) ALLYMFDNELPDCNQVRVAIOLGGATWLTHEDTEDLGVIIISFG
           Consensus  (421) YDTAILFTRQDLCG  G CDTLGMADVGT CDP RSC VIEDDGLQQAFT AHELGHVLG
                    481                                                          540
hADAMTS-4 (AB014588)  (369) LFSSKPCINMLSTSRHVARVMAHVDPEEPRPSARFIDPEDNGYGHDLK
hADAMTS-5 (AF142099)  (417) LSDSNFCETFSTE-DKRLSIITSIDASKFKISATIREDDHCNLLL
hADAMTS-1 (AF060152)  (392) MPDAKQCASIN-VNQDSHMEASMLSNIHSQPSYMISDNGHCELMLK
hADAMTS-8 (AF060153)  (372) MPDSNPCTLFPMG-KHHVALRLFVHLNQTLPSPSAMYDEFDGHCGDHA
hADAMTS-2 (AJ003125)  (416) MECGG--NRCDEVRLGSIELVQAAFHRFHIRSQQEDSRYHS--YDLMDD
              M1-MPD  (158) UECAP--GSGCPSG---HVMSDGAAPRAGLAIFSRRQHLSISAGARYVMP
           Consensus  (481) M HDDSK C SL GP   HVMAS    D  PWSPCSA  LT FLD GHG CLLD P
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                                               541                                                           600
hADAMTS-4 (AB014588)   (429) EAP--LHLPVTFPG--KDVLADRCQIFFGPDSRHCP--QLPPPCAAICSGHLNGHAMC
hADAMTS-5 (AF142099)   (476) RKQ--ILGEEIPG--QTLLETCQCNLLFGPEYSVCR--GMDVCRHCAVRCQSQMVC
hADAMTS-1 (AF060152)   (451) QNP--IQEEGDLPG--TSNDANRCCFTEGEDSKHCP--DAASTCSTWCTGTSGGVLVC
hADAMTS-8 (AF060153)   (431) GAA--LPLETGHGRMALCLDQQRQIEGDFRHCINTSAQDVCAQIWCH-TDGAEPLC
hADAMTS-2 (AJ003125)   (471) FAHDWPALP-QLPG--LHLSVNECCRFDFGLGYMMCTAFRTFDPCKQIWCS-HPDNPYFC
            M1-MPD     (213) RP-------------------------------------------------------
          Consensus    (541) A    LP LPG    YDA    QC    TFGPD  HCP    D CA LWC    G    C
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